



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

Journal of Acute Disease

journal homepage: www.jadweb.org



Document heading doi:

Horizontal transmission of novel H1N1/09 influenza virus in a newborn: Myth or fact?

Uttam Kumar Sarkar¹, Utpala Mitra², Mamta Chawla Sarkar², Shanta Dutta², Himanish Roy¹, Mrinal Kanti Chatterjee¹, Phalguni Dutta^{2*}

¹Department of Pediatric Medicine, Dr. B.C. Roy Memorial Hospital for Children, 111, Narkeldanga Main Road, Kolkata–700054, India

²National Institute of Cholera and Enteric Diseases, P33 CIT Road, Scheme XM, Beliaghata, Kolkata–700010, India

ARTICLE INFO

Article history:

Received 10 January 2012

Received in revised form 15 March 2012

Accepted 15 May 2012

Available online 20 November 2012

Keywords:

Newborn

Pandemic H1N1/09

Horizontal transmission

Respiratory droplets

ABSTRACT

Horizontal transmission of H1N1/09 virus infection is very common however; transmission through this route has not been reported in newborns. To our knowledge, this is the first case report of newborn who acquired infection of novel H1N1/09 virus horizontally through asymptomatic family members or hospital staff during epidemic period in Kolkata, India. Baby recovered without antiviral therapy but received antibiotic for bacterial co-infection.

1. Introduction

Pandemic H1N1/09 influenza virus infection has been identified as the cause of a wide spread outbreak of febrile respiratory infection worldwide[1]. Pandemic H1N1/09 infection also swept throughout India[2]. In the wake of the pandemic, a newborn infected with novel H1N1/09 influenza virus admitted to a teaching hospital in Kolkata, India who acquired infection through person to person contacts or by respiratory droplets. Spread of this infection through these routes is very common in older children and adults[1] however; it was not yet reported in newborns. In contrast, vertical transmission of H1N1/09 infection from pregnant women to the newborns has been published during the pandemic period[3–5].

2. Case report

A male infant was born to a 21 year-old– mother at 36 weeks gestation and weighed 2 200 g by normal vaginal delivery at hospital set up on 9th July, 2010. Apgar scores were 9 both at 1 and 5 min. The mother did not have significant past medical history of respiratory infection for last one month. She did not recall any contacts with ill individuals and denied recent travel. Mother and baby were discharged from hospital on next day of delivery. Baby was looked after by his mother and was exclusive breast fed up to day 4. However, mother developed severe dehydrating diarrhea and admitted to another hospital on day 5. Baby was at home and developed fever, occasional cough and vomiting on that day. Baby became lethargic and developed respiratory distress on day 6 for which he was admitted to the hospital on day 7.

On physical examination, the baby was weighed 1 800 g and had high grade of fever (39 °C) with respiratory distress. Respiratory rate was 66/min and respiration was mainly

*Corresponding author: Dr. Phalguni Dutta, Emeritus Medical Scientist (ICMR), Former Scientist–G (Director Grade Scientist), National Institute of Cholera and Enteric Diseases, P33 CIT Road, Scheme XM, Beliaghata, Kolkata–700010, India.

Tel: 91–33–2363 3554

Fax: 91–33–23632398

E-mail: drpdutta@yahoo.com

abdominal. Silverman scoring for gradation of respiratory distress was 3. Few crepts were detected on auscultation in both the lungs. Chest radiograph revealed hyper inflated lungs. Hematological examinations showed the following: hemoglobin 12.1 g/dL, total leucocytes–26 800/mm³, differential count (cells/μL of blood): lymphocytes 7 236, neutrophil 18 760, eosinophil 536, monocytes 268, platelet count 101 000 mm³. Estimation (mg/dL) of conjugated, un-conjugated bilirubin and C-reactive protein showed 16, 4 and 24 respectively. Other systems were within normal limit.

As the baby was admitted during the epidemic period, nasopharyngeal swab specimens collected on day 7 and 8 were examined for pandemic H1N1/09 using the standard CDC methodology[6]. Extraction of viral RNA from the clinical samples was carried out using commercially available QiaAmp Viral RNA Mini Kit (Qiagen, GmbH, Hilden, Germany) according to the manufacturer's instruction. One-step Real-time RT-PCR assay was performed using TaqMan Influenza Assay Kit (Part No. 4401512, Applied Biosystems, Foster City, USA) and AgPath-ID One-Step RT-PCR Kit (Part No.4387391, Ambion, Austin, USA) for diagnosis of pandemic H1N1. Each sample was subjected to four reactions testing for influenza A matrix (M) gene, pandemic H1N1 nucleoprotein (NP), pandemic H1N1 hemagglutinin (HA1) gene and human gene RNase P as an internal control[6]. After receiving positive result of H1N1/09 of the baby, nasopharyngeal swabs of both the parents and grandparents were also examined which were negative for H1N1/09.

The baby was put on intravenous antibiotics (cefotaxim and amikacin) empirically. Fluid and electrolyte balance was maintained intravenously and subsequently by nesogastic feeding till the baby became breast fed. Baby was on supportive therapy with moist oxygen supplementation and paracetamol. However, temperature continued till day 14 but repeat examination of nasopharyngeal swab showed elimination of pandemic H1N1/09. Due to continued fever, blood sample was collected aseptically to detect bacterial pathogen on day 15 using standard technique. *Klebsiella pneumoniae* (*K. pneumoniae*) was grown in blood culture after 24 h of incubation. The antimicrobial susceptibility of this isolate was determined by Kirby Bauer's disc diffusion method using a panel of commercially available discs (Beckton Dickenson, MD, USA). Minimum Inhibitory Concentrations (MICs) of the antibiotics for this isolate were determined by E-test strips (AB BIODISK, Solna, Sweden) according to manufacturer's recommendations. *E. coli* ATCC 25922 was used as a reference strain for quality control checking. Results were interpreted as per Clinical Laboratory Standard Institute guidelines[7]. The isolate was susceptible to chloramphenicol, tetracycline, amikacin, nalidixic acid, norfloxacin, ciprofloxacin, ofloxacin, levofloxacin,

gatifloxacin, imipenem and meropenem but resistant to the following antimicrobials with their MICs: ampicillin (>256 μ L/mL), piperacillin (>256 μ L/mL), co-trimoxazole (>32 μ L/mL), cefotaxime (>256 μ L/mL), ceftazidime (>256 μ L/mL), ceftriaxone (>256 μ L/mL), cefpodoxime (>256 μ L/mL), cefipime (>256 μ L/mL), cefixime (>256 μ L/mL), azithromycin (>256 μ L/mL), aztreonam (>256 μ L/mL). The isolate was shown to be positive for Extended Spectrum of Beta Lactamase (ESBL) by phenotypic test.

We changed the antibiotics to meropenem (60 mg/kg/d in three divided doses) on day 18 as the isolates of *K. pneumoniae* was susceptible to that drug and continued for 12 d. No antiviral drug was given. On day 23, baby became afebrile and respiratory distress subsided without any complication. Baby was stable, had breast milk and gained weight during hospital stay. Baby was discharged from the hospital on day 30. The baby was also doing well during subsequent follow up visit at the age of two months.

3. Discussion

Failure of detection of H1N1/09 infection in neonates during the epidemic period in Hong Kong[8], indicated that it is still a myth that neonates have some specific mechanism that brings resistant to this respiratory infection[9]. However experts opined that there are many more cases of neonatal H1N1/09 infection elsewhere in the world[10], but there is no published document of horizontal transmission of H1N1 infection in neonates till date. To our knowledge, this is the first case report of seven days old newborn who acquired H1N1/09 infection horizontally through person to person close contacts or by respiratory droplets though this route of transmission is very common among older children and adults[1]. Earlier reports documented vertical transmission of H1N1/09 infection from their mothers[3–5] though transmission by this route was thought to be rare[11].

Baby was well till day 6 of birth and the prenatal and immediate postnatal periods of his mother were uneventful indicated that he did not acquired infection vertically. However, mother developed severe dehydrating diarrhea in later half of postnatal period but her nasopharyngeal swab was negative for H1N1/09 which negated the possibility of H1N1/09 related diarrhea in mother and possibility of transmission of infection to the baby. During pandemic, a good proportion of pediatric inpatients were positive for H1N1/09 in USA but none was in neonatal age group[12]. Neonates suffering from respiratory infection were screened for H1N1/09 infection during the epidemic period in Hong Kong which showed that H1N1/09 did not appear to be the prevalent respiratory virus in neonates[8].

Probably the baby acquired the infection through person to person close contacts or by respiratory droplets at home from other asymptomatic family members except parents and grandparents as they were negative for H1N1/09. To avoid transmission, direct caregivers along with other family members and visitors should also pay special attention to personal and hand hygiene whenever they are in close contact of the newborns.

Possibility of transmission of this infection from the hospital staff during delivery or during post delivery care cannot be ignored as seropositivity of H1N1/09 among hospital staff was high in different countries including India^[13]. Hospital staffs should receive health education regarding infection control practices due to presence of high percentage of asymptomatic subjects in the community and they became the potential source of infection^[2,13]. Health authority should take appropriate preventive measures to minimize the spread of infection.

We initiated treatment of this febrile newborn with cefotaxim and amikacin empirically but the baby had continued fever till day 17 even after elimination of H1N1/09. Bacteriological report of blood culture showed presence of multidrug resistant *K. pneumonia* which explained no response of initial combined therapy however baby responded with meropenem as the stain was highly susceptible to that drug. World Health Organization (WHO) also recommended use of antibiotic empirically as H1N1/09 infections are usually associated with bacterial co-infection in children including neonates in developing countries^[14]. Antibiotic therapy became an integrated part of treatment of H1N1 to combat bacterial co-infection in newborns in developing countries like ours^[14].

We did not use any antiviral agent to this newborn as routine antiviral therapy was not recommended by WHO to all H1N1/09 infected patients^[14]. Furthermore, the use of antiviral agents in newborns is problematic and not regarded as safe^[8]. Elimination of this infection without antiviral therapy indicated that antiviral agent may not be required for all H1N1/09 infected cases.

In conclusion, it is fact that newborn can be infected with H1N1/09 virus and the transmission can be occurred horizontally even by asymptomatic contacts. Special attention to personal as well as hand hygiene among the close contacts of newborns is the main public health importance to avoid the transmission of this infection.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

References

- [1] Zarocostas J. World Health Organization declares A (H1N1) influenza pandemic. *BMJ* 2009; **338**: b2425. doi: 10.1136/bmj.b2425.
- [2] Mishra AC, Chadha MS, Choudhary ML, Potdar VA. Pandemic Influenza (H1N1) 2009 is associated with severe disease in India. *PLoS One* 2010; **5**(5): e10540.
- [3] Sert A, Yazar A, Odabas D, Bilgin H. An unusual cause of fever in a neonate: Influenza A (H1N1) virus pneumonia. *Pediatr Pulmonol* 2010; **45**: 734–736. doi: 10.1002/ppul.21245
- [4] Fridman D, Kuzbari O, Minkoff H. Novel influenza H1N1 in pregnancy: A report of two cases. *Infect Dis Obstetr Gynecol* 2009; 514353. doi: 10.1155/2009/514353
- [5] Dulyachai W, Makkoch J, Rianthavorn P, Changpinyo M, Prayangprecha S, Payungporn S, et al. Perinatal pandemic (H1N1) 2009 infection, Thailand. *Emer Infect Dis* 2010; **10**: 343–344.
- [6] CDC protocol of realtime RTPCR for swine influenza A (H1N1) pr 2009. CDC REF. #I-007-05. Page 2 of 8. Version 2009.
- [7] NCCLS. *Performance Standards for Antimicrobial Susceptibility Test Approved Standards, 8th edn. NCCLS Document M2-A8*. NCCLS: Wayne, PA; 2003.
- [8] Hon KL, Cheung KL, Wong W, Ng PC. Neonates investigated for influenza-like illness during the outbreak of pandemic H1N1 2009: trivial infections but major triage implications. *Indian J Pediatr* 2010; **77**: 1033–1035.
- [9] Wiwanitkit V. Pandemic H1N1 2009 in neonates (Letter). *Indian J Pediatr* 2011; **78**: 120.
- [10] Hon KL. Pandemic H1N1 2009 in neonates (Letter). *Indian J Pediatr* 2011; **78**: 120.
- [11] Shek CC, Ng PC, Fung GPG, Cheng FWT, Chan PKS, Peris MJS, et al. Infants born to mothers with severe acute respiratory syndrome. *Pediatr* 2003; **112**: e254–e256. Doi:10.1542/peds.112.4.e254
- [12] Tamma PD, Turnbull AE, Milstone AM, Cosgrova SE, Valsamakis A, Budd A, et al. Clinical outcomes of seasonal influenza and pandemic influenza A (H1N1) in pediatric inpatients. *BMC Pediatr* 2010; **10**: 72. doi: 10.1186/1471-2431-10-72.
- [13] Tandale BV, Pawar SD, Gurav YK, Chadha MS, Karatkar SS, Shelke VN, et al. Seroepidemiology of pandemic influenza A (H1N1) 2009 virus infections in Pune, India. *BMC Infect Dis* 2010; **10**: e255. doi: 10.1186/1471-2334-10-255
- [14] World Health Organization. Clinical management of human infection with new influenza (H1N1) virus: initial guidance. [Online]. Available from: www.emro.who.int/csr/h1n1/pdf/clinical [Accessed on May 21, 2009].